

CONDITIONED MEDIUM AND EXTRACELLULAR MATRIX COMPOSITIONS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of priority under 35 U.S.C. § 119(e) of U.S. Ser. No. 62/713,984, filed Aug. 2, 2018, the entire contents of which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

[0002] The present invention relates generally to the production and use of growth factors and/or conditioned culture medium compositions and more specifically to compositions for hair, lash and/or nail growth.

Background Information

[0003] The extracellular matrix (ECM) is a complex structural entity surrounding and supporting cells that are found in vivo within mammalian tissues. The ECM is often referred to as the connective tissue. The ECM is primarily composed of three major classes of biomolecules including structural proteins such as collagens and elastins, specialized proteins such as fibrillins, fibronectins, and laminins, and proteoglycans. Conditioned culture medium (CCM) contains biologically active components obtained from previously cultured cells or tissues that have released into the media substances affecting certain cell function. It has been found that ECM and CCM compositions derived in vitro from cells grown under hypoxic or normoxic conditions have therapeutic properties beneficial for treating certain conditions.

[0004] Growth of ECM compositions in vitro and their use in a variety of therapeutic and medical applications have been described in the art. One therapeutic application of such ECM compositions includes treatment and repair of soft tissue and skin defects such as wrinkles and scars.

[0005] The repair or augmentation of soft tissue defects caused by defects, such as, acne, surgical scarring or aging has proven to be very difficult. A number of materials have been used to correct soft tissue defects with varying degrees of success, however, no material has been completely safe and effective. For example, silicon causes a variety of physiological and clinical problems including long term side effects, such as nodules, recurring cellulitis and skin ulcers.

[0006] Collagen compositions have also been used as an injectable material for soft tissue augmentation. Collagen is the main protein of connective tissue and the most abundant protein in mammals, making up about 25% of the total protein content. There are currently 28 types of collagen described in literature (see, e.g., Tables 1 and 2 *infra*, for a detailed listing). However, over 90% of the collagen in the body are Collagens I, II, III, and IV.

[0007] Different collagen materials have been used for treatment of soft tissue defects, such as reconstituted injectable bovine collagen, crosslinked collagen, or other xenogeneic collagens. However, several problems exist with such collagens. A common problem includes the complexity and high cost of producing the implant materials to remove potentially immunogenic substances to avoid allergic reac-

tions in the subject. Additionally, treatments using such collagens have not proven long lasting.

[0008] Other materials have also been described that may be used for soft tissue repair or augmentation, such as, biocompatible ceramic particles in aqueous gels (U.S. Pat. No. 5,204,382), thermoplastic and/or thermosetting materials (U.S. Pat. No. 5,278,202), and lactic acid based polymer blends (U.S. Pat. No. 4,235,312). Additionally, use of naturally secreted ECM compositions have also been described (U.S. Pat. No. 6,284,284). However, such materials have all proven to have limitations.

[0009] In vitro cultured ECM compositions can additionally be used to repair and/or regenerate damaged cells or tissue, such as chondral or osteochondral cells. Osteochondral tissue is any tissue that relates to or contains bone or cartilage. The compositions of the present invention are useful for treatment of osteochondral defects, such as degenerative connective tissue diseases, such as rheumatoid and/or osteoarthritis as well as defects in patients who have cartilage defects due to trauma.

[0010] In vitro cultured ECM compositions are also useful in tissue culture systems for generation of engineered tissue implants. The field of tissue engineering involves the use of cell culture technology to generate new biological tissues or repair damaged tissues. Fueled in part, by the stem cell revolution, tissue engineering technology offers the promise of tissue regeneration and replacement following trauma or treatment of degenerative diseases. It can also be used in the context of cosmetic procedures.

[0011] Culture medium compositions typically include essential amino acids, salts, vitamins, minerals, trace metals, sugars, lipids and nucleosides. Cell culture medium attempts to supply the components necessary to meet the nutritional needs required to grow cells in a controlled, artificial and in vitro environment. Nutrient formulations, pH, and osmolarity vary in accordance with parameters such as cell type, cell density, and the culture system employed. Many cell culture medium formulations are documented in the literature and a number of media are commercially available. Once the culture medium is incubated with cells, it is known to those skilled in the art as “spent” or “conditioned medium”. Conditioned medium contains many of the original components of the medium, as well as a variety of cellular metabolites and secreted proteins, including, for example, biologically active growth factors, inflammatory mediators and other extracellular proteins. Cell lines grown as a monolayer or on beads, as opposed to cells grown in three-dimensions, lack the cell—cell and cell-matrix interactions characteristic of whole tissue in vivo. Consequently, such cells secrete a variety of cellular metabolites although they do not necessarily secrete these metabolites and secreted proteins at levels that approach physiological levels. Conventional conditioned cell culture medium, medium cultured by cell-lines grown as a monolayer or on beads, is usually discarded or occasionally used in culture manipulations such as reducing cell densities.

[0012] The majority of vertebrate cell cultures in vitro are grown as monolayers on an artificial substrate bathed in culture medium. The nature of the substrate on which the monolayers grow may be solid, such as plastic, or semisolid gels, such as collagen or agar. Disposable plastics have become the preferred substrate used in modern-day tissue or cell culture.